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UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

ARIOSA DIAGNOSTICS, INC., Plaintiff, v. SEQUENOM, INC., Defendant/ Counterclaim-Plaintiff, v. ARIOSA DIAGNOSTICS, INC., Counterclaim-Defendant, and ISIS INNOVATION LIMITED, Nominal Counterclaim-Defendant.	Case No. 3:11-cv-06391-SI **SEQUENOM'S OPPOSITION TO ARIOSA'S MOTION FOR SUMMARY JUDGMENT, CROSS-MOTION FOR PARTIAL SUMMARY JUDGMENT ON SECTION 101 PATENT ELIGIBILITY, AND MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF CROSS-MOTION** Date: October 11, 2013 Time: 9:00 a.m. Place: Courtroom 10, 19th Floor Judge: Hon. Susan Illston

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NOTICE OF CROSS-MOTION AND CROSS-MOTION

TO ALL PARTIES AND TO THEIR COUNSEL OF RECORD:

PLEASE TAKE NOTICE that, pursuant to the Court's Order entered on August 27, 2013, on October 11, 2013, at 9:30 a.m., in the courtroom of the Hon. Susan Illston, located at 450 Golden Gate Avenue, San Francisco, California, Defendant and Counterclaim-Plaintiff Sequenom, Inc. will cross-move, and does now move, for an order of partial summary judgment pursuant to Rule 56 of the Federal Rules of Civil Procedure against the third affirmative defense ("Invalidity") of Plaintiff and Counterclaim-Defendant Ariosa Diagnostics, Inc. that Sequenom's United States Patent No. 6,258,540 is not drawn to patentable subject matter pursuant to 35 U.S.C. § 101.

Sequenom makes this cross-motion for partial summary judgment based on the pleadings, the Memorandum of Points and Authorities filed concurrently with this Notice, the accompanying Declaration of Peter E. Root and the attached exhibits, the [Proposed] Order submitted with this Notice, and any other further papers and argument which may be submitted to the Court in connection with Ariosa's motion for summary judgment and this cross-motion for partial summary judgment.

Dated: September 4, 2013

Respectfully submitted,

KAYE SCHOLER LLP

By: */s/ Peter E. Root*
Peter E. Root
Attorneys for Defendant
SEQUENOM, INC.

I. INTRODUCTION.

Patent 6,258,540 ("the '540 patent") does not claim a natural phenomenon. To be sure, the '540 patent's inventors, Dr. Lo and Dr. Wainscoat, discovered that cell-free fetal DNA ("cffDNA") is detectable in maternal plasma or serum, but the '540 patent does not claim that natural phenomenon. Rather, the '540 patent claims specific variations of their method for (1) separating a plasma or serum sample from maternal blood; (2) amplifying paternally inherited nucleic acid from that sample; and (3) detecting paternally inherited fetal nucleic acid in that sample. The '540 patent inventors found that this particular combination of steps provided a new and practical method of detecting *fetal* genetic characteristics through analysis of a *maternal* blood sample. The '540 patent does not preempt other methods that make use of cffDNA.

This Court should find as a matter of law that the '540 patent claims a patent-eligible method. The Court should reach that conclusion for the following reasons:

First, Section 101 of the Patent Act provides in expansive terms for the patenting of "***any*** new and useful process." The judicially-created exceptions to patentability – including the exception for a natural phenomenon – must be narrowly construed. Anyone asserting invalidity under Section 101 must present clear and convincing evidence to support the challenge. Ariosa has failed to do that.

Second, the prohibition against patenting of a natural phenomenon does not prevent patenting of novel *uses* of a natural phenomenon. Before Drs. Lo and Wainscoat invented a method for detecting paternally inherited *fetal* DNA in *maternal* plasma, researchers involved in non-invasive prenatal DNA diagnosis methods had thrown away the non-cellular fraction as useless. Having discovered that cffDNA could be detected in maternal plasma and serum, Drs. Lo and Wainscoat "[a]s the first party with knowledge of" the presence of cffDNA in maternal plasma and serum, were "in an excellent position to claim applications of that knowledge." *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2120 (2013). The '540 patent's method – by making use of what had previously been discarded as waste – was a novel and inventive application of the natural phenomenon.

Ariosa's counter-argument rests largely upon its misreading of *Mayo Collaborative Serv.v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012), the same argument it unsuccessfully made trying to persuade the Federal Circuit to affirm this Court's denial of Sequenom's preliminary injunction. Had the Federal Circuit believed that *Prometheus* raised a "substantial question" of patent eligibility, it could have affirmed on that ground. Instead, the Federal Circuit directed this Court to re-consider the subject matter eligibility of the'540 patent "in light of" the Supreme Court's later decision in *Myriad* and "also in light of this [Federal Circuit] court's disagreement with the district court's claim construction." *Aria Diagnostics, Inc. v. Sequenom, Inc.*, __ F.3d __, 2013 WL 4034379 at *6 (Fed. Cir. Aug. 9, 2013) ("*Aria*"). Ariosa's brief makes no reference to the Federal Circuit's opinion, refers only perfunctorily to *Myriad*, and instead rehashes the pre-*Myriad* legal arguments that did not persuade the appellate panel. The holding and teaching of *Myriad* defeat Ariosa's summary judgment motion.

Third, the claims of the '540 patent are patent eligible because they do not preempt all uses of cffDNA. Both the unanimous Supreme Court in *Myriad* and the *en banc* Federal Circuit in *CLS Bank Int'l v. Alice Corp. Pty. Ltd.*, 717 F.3d 1269 (Fed. Cir. 2013), emphasized that a patent passes muster under Section 101 as long as it does not preempt all uses of a natural phenomenon, law of nature, or abstract idea. While pioneering, Dr. Lo's and Dr. Wainscoat's invention does not monopolize all methods of using cffDNA. Other methods for using cffDNA have been described in peer-reviewed, scientific journals including methods that use cffDNA (1) without starting with maternal plasma or serum; (2) without amplification of fetal DNA; or (3) without detecting paternally-inherited fetal DNA. Because each of the steps of the '540 patent, when construed in accordance with the Federal Circuit's recent opinion in this case, provides a meaningful limitation to the use of cffDNA claimed by the patent, the patent does not monopolize all uses of that phenomenon.

Fourth, Ariosa devotes most of its brief to its misguided effort to establish that each of the three fundamental steps in the '540 patent was "well-known in the art" at the time of the invention. The Supreme Court and the Federal Circuit have repeatedly rejected this approach to Section 101 analysis. Every patent can be stripped down piece by piece to a law of nature,

natural phenomenon, or abstract idea at its core, but this piecemeal dissection of the claimed method is not the test for patent eligibility. Drs. Lo and Wainscoat were awarded the '540 patent because they combined previously-known steps into a never-before-devised method that led them, first, to discover cffDNA in maternal plasma and serum and, then, to use their inventive method as a non-invasive tool for prenatal diagnostics. This inventive combination makes the '540 patent's method patent-eligible subject matter.

For all of these reasons, the Court should hold as a matter of law that the '540 patent is eligible under Section 101. Accordingly, the Court should deny Ariosa's motion for summary judgment and grant Sequenom's cross-motion for partial judgment on Ariosa's Section 101 affirmative defense.

II. FACTUAL BACKGROUND.

In 1996, Dr. Dennis Lo and Dr. James Wainscoat, working at Oxford University, created "a paradigm shift in non-invasive prenatal diagnosis." A1115, ¶ 52.[1] Before their discovery, researchers had long tried to develop approaches to prenatal diagnosis that would avoid invasive procedures, such as amniocentesis, that pose a risk to the fetus. A1110-1111, ¶¶ 38-40. The most promising and most pursued approach focused on isolating rare fetal nucleated cells that had escaped from the amniotic sac into the mother's bloodstream. *Id.*; *see generally Aria*, 2013 WL 4034379 at * 1. Drs. Lo and Wainscoat took a radically different and counter-intuitive approach. A1102, ¶¶ 20-21; A1118-1119, ¶ 70.

Their work yielded the unexpected and landmark invention of an innovative method to detect fetal characteristics through analysis of fetal nucleic acids circulating outside of cells – so-called "cell-free fetal DNA and RNA" – in pregnant women's blood. A1111, ¶ 41; A1115, ¶¶ 52-53; A1119, ¶ 71; A1908-1942. "In other words, the '540 patent claims methods to detect fetal genetic characteristics by analyzing cffDNA obtained from a maternal blood sample." *Aria* at *1.

[1] References to "A" and a number refer to pages from the Joint Appendix of evidence the parties submitted to the Federal Circuit for the appeal of this Court's July 2, 2012 preliminary injunction order. The pages cited in this brief are copied and attached as Exhibit A to the Declaration of Peter Root filed concurrently with Sequenom's cross-motion for summary judgment.

The '540 patent claims specific variations of that method, all of which involve the novel application and innovative combination of three distinct steps:

(1) separating or fractionating maternal blood to produce a plasma or serum sample;

(2) amplifying a paternally inherited nucleic acid from the plasma or serum sample; and

(3) detecting a paternally inherited fetal nucleic acid in the plasma or serum sample.

A37, 23:61-67. Those three steps are found in claim 1 of the patent, on which all of the other claims of the patent are dependent, except for claims 24 and 25, which themselves recite variations of those three steps.

Drs. Lo and Wainscoat first used this method to test their hypothesis that the plasma of a pregnant mother contained cell-free DNA from the fetus she was carrying. The '540 patent inventors then found that this particular combination of steps provided a new and practical method of detecting a wide range of *fetal* genetic characteristics through analysis of a *maternal* blood sample. A26, 1:50-2:18. Before Lo's and Wainscoat's invention, no one had used the cell-free fraction of maternal blood for prenatal diagnosis. *See* A26, 1:24-67. Indeed, earlier researchers had thrown away the cell-free fraction as useless. A1118-1119, ¶ 70. As the Federal Circuit explained, "[t]he '540 patent discloses methods to identify fetal genetic defects by analyzing the fluid that had commonly been discarded as medical waste – the maternal plasma or serum." *Aria* at *1.

The three-step method in the '540 patent enabled Lo and Wainscoat to distinguish fetal cell-free DNA from the mother's own cell-free DNA. In the prior art, researchers had searched for rare fetal cells in the mother's bloodstream so that they could then conduct tests on the purely fetal DNA within the fetal cells. *See* '540 patent at 1:26-37. In an original stroke of genius, Lo and Wainscoat searched for a more abundant source of fetal DNA in the mother's plasma or serum, *see Aria* at *1, and, in another insight, focused on paternally inherited fetal DNA that differed from the mother's own DNA. A26, 2:57-59; A1887, ¶ 73. With a series of experiments that looked for pieces of the Y chromosome and RhD gene in mothers ostensibly lacking that

gene, they proved that their method could detect the paternally inherited cffDNA in maternal plasma or serum.

As the '540 patent's specification explains, "[t]he method according to the invention can be applied to the detection of any paternally-inherited sequences which are not possessed by the mother . . . ." A26, 2:57-59. The patented method aims to detect those paternally inherited sequences found in a pregnant mother's plasma or serum. A37, 23:60-67. The Federal Circuit has construed this claimed method to include detection of sequences which are not known in advance to come from the father. *Aria* at * 3-5. The patent's specification explains how to perform the invention, and sets forth examples of diagnostic methods. Those methods include a quantitative approach for detecting chromosomal abnormalities, such as Down syndrome, and fetal RhD genotyping, which was "the first description of single gene diagnosis from maternal plasma." A26, 2:1-12, 8:51-11:35.

The scientific community recognized the method embodied in the '540 patent as unconventional, non-routine, transformative, and groundbreaking. A1118-1119, ¶¶ 69-71. These non-invasive methods have revolutionized prenatal diagnostics. A1069-1070, ¶¶ 9-12; A1113-1115, ¶¶ 45-54; A1119, ¶ 71.

III. ARGUMENT.

A. PATENTS ARE PRESUMED VALID, AND CLEAR AND CONVINCING EVIDENCE IS REQUIRED TO INVALIDATE A PATENT UNDER SECTION 101.

Section 101 of the Patent Act provides:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

35 U.S.C. § 101. "In choosing such expansive terms . . . modified by the comprehensive 'any,' Congress plainly contemplated that the patent laws would be given wide scope." *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010) (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980)).

The three judicially created exceptions to the sweeping language of Section 101 – natural phenomena, laws of nature, and abstract ideas – must be applied "narrowly." *Bilski*,130 S. Ct. at 3225, 3229. Further, "to override the broad statutory categories of eligible subject matter," the "disqualifying characteristic" of an exception to Section 101 must exhibit itself "manifestly." *Research Corp. Techs., Inc. v. Microsoft Corp.*, 627 F.3d 859, 868 (Fed. Cir. 2010).

Validity or invalidity under Section 101 is determined as a matter of law. *See CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1369 (Fed. Cir. 2011); *see also Oleksy v. General Electric Co.* , 2013 WL 3233259 at *1, 3 (N.D. Ill. June 26, 2013) (determining cross-motions for summary judgment as matter of law post-*Myriad*).

The presumption of validity that applies to every patent applies equally to the patent's validity under Section 101. *Ultramercial, Inc. v. Hulu, LLC,* __ F.3d __, 2013 WL 3111303 at *2 (Fed. Cir. June 21, 2013), *petition for cert. filed* (U.S. August 23, 2013) (No. 13-255). Accordingly, "any attack on an issued patent based on a challenge to the eligibility of the subject matter must be proven by clear and convincing evidence." *CLS Bank*, 717 F.3d at 1304-05.

As the five-judge plurality of the Federal Circuit in *CLS Bank* explained, "it bears remembering that all issued patent claims receive a statutory presumption of validity," and "that presumption applies when § 101 is raised as a basis for invalidity in district court proceedings." 717 F.3d at 1284. The four-judge concurring opinion of Chief Judge Rader connected this presumption to the burden of proof: "Because we believe the presumption of validity applies to all challenges to patentability, including those under Section 101 and the exceptions thereto, we find that any attack on an issued patent based on a challenge to the eligibility of the subject matter must be proven by clear and convincing evidence." *Id.* at 1304-05. *See also Ultramercial*, 2013 WL 311103 at *2 (in resolving Section 101 issues, "every issued patent is presumed to have been issued properly, absent clear and convincing evidence to the contrary").

Patent eligibility under Section 101 may be resolved on cross-motions for summary judgment. Before it reached the Federal Circuit and Supreme Court, *Myriad* was first decided in the district court on cross-motions for summary judgment. *See Ass'n for Molecular Pathology v. United States Patent and Trademark Office*, 702 F. Supp. 2d 181, 184-85 (S.D.N.Y. 2010). The

Federal Circuit's *en banc* decision in *CLS Bank* also reviewed the outcome of cross-motions for summary judgment on the Section 101 issue. *See CLS Bank*, 717 F.3d at 1275. Cross-motions for summary judgment likewise was the procedure by which the district court resolved the most recently reported post-*Myriad* case deciding a Section 101 patent eligibility issue. *See Oleksy*, 2013 WL 3233259 at *1, 20 (denying alleged infringer's summary judgment motion to invalidate patent under Section 101 and granting patentee's cross-motion for summary judgment on Section 101 defense). *See also Chamberlain Group, Inc. v. Lear Corp.*, 756 F. Supp.2d 938, 969 (N.D. Ill. 2010) (deciding cross-motions for summary judgment on Section 101 defense); *Lusa Lighting, Int'l, Inc. v. America Elex, Inc.*, 2008 WL 4350741 at *6 (C.D. Cal. 2008) (same).

B. APPLYING THE FEDERAL CIRCUIT'S DIRECTIONS, THE '540 PATENT MEETS SECTION 101 BECAUSE IT CLAIMS AN INVENTIVE METHOD TO DETECT A NATURAL PHENOMENON, BUT DOES NOT CLAIM THE NATURAL PHENOMENON ITSELF.

1. The Use Of cffDNA Is Patent Eligible.

The '540 patent claims a "new and useful process," as that term is used in Section 101. Before the ground-breaking work of Drs. Lo and Wainscoat, the state of the art for non-invasive prenatal diagnosis was to search for rare fetal cells in the pregnant mother's blood stream. Researchers had *thrown away* the non-cellular fraction as waste. *Aria* at *1 ("Once the cells were separated, the remaining maternal serum or plasma was commonly discarded as waste . . . ."). Ariosa can offer no evidence that *anyone* prior to Lo and Wainscoat had *ever* used cffDNA for prenatal genetic diagnosis. Indeed, all of the evidence is to the contrary.

Certainly, no one had started with pregnant mother's plasma or serum to detect paternally inherited fetal DNA, as required by the specific methods claimed by the '540 patent. But once Drs. Lo and Wainscoat invented a method to (a) start with maternal serum or plasma separated from the cellular portion of the maternal blood, (b) amplify paternally inherited fetal nucleic acids, and (c) detect paternally inherited fetal nucleic acid, the world beat a path following in their footsteps. Even Ariosa's expert, Dr. Farideh Bischoff, whose research had previously been

focused on the rare fetal cells found in pregnant mothers' blood, promptly switched to using cell-free fetal DNA after learning of Drs. Lo's and Wainscoat's breakthrough.[2]

The '540 patent *does not* claim the natural phenomenon of cell-free fetal DNA. The patent *does* claim specific methods for using cffDNA consisting of starting with maternal plasma or serum and amplifying and detecting paternally inherited fetal DNA, resulting in characterization of fetal genetic makeup.

While natural phenomena, laws of nature, and abstract ideas are not themselves patentable, "[a] process is not unpatentable simply because it contains a law of nature or a mathematical algorithm." *Prometheus*, 132 S. Ct. at 1293-94 (quoting *Diamond v. Diehr*, 450 U.S. 175, 187 (1981)). As the Supreme Court held 65 years ago, while a natural phenomenon is not patentable, an invention can "come from the application of the law of nature to a new and useful end." *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948); *accord Gottschalk v. Benson*, 409 U.S. 63, 67 (1972). The judicially created exception under Section 101 prohibiting patents on natural phenomena is "not without limits" because "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas," and "too broad an interpretation of this exclusionary principle could eviscerate patent law." *Myriad*, 133 S. Ct. at 2116 (internal quotations omitted).

[2] *Compare* Farideh Z. Bischoff et al., *Detection of Low-Grade Mosaicism in Fetal Cells Isolated from Maternal Blood*, 15 Prenatal Diagnosis 1099, 1182-1184 (1995) and Farideh Z. Bischoff et al., *Prenatal Diagnosis with Use of Fetal Cells Isolated from Maternal Blood: Five-Color Fluorescent In Situ Hybridization Analysis on Flow-Sorted Cells for Chromosomes X, Y, 13, 18, and 21*, 179 Am. J. Obstetrics & Gynecology 1, 203-209 (July 1998) *with* Farideh Z. Bischoff at al., *Noninvasive Determination of Fetal RhD Status Using Fetal DNA in Maternal Serum and PCR*, 6 J. Soc'y Gynecologic Investigation 56, 64-69 (1999) and Farideh Z. Bischoff at al., *Cell-Free Fetal DNA and Intact Fetal Cells in Maternal Blood Circulation: Implications for First and Second Trimester Non-Invasive Prenatal Diagnosis*, 8 Human Reproduction Update 493, 493-500 (2002) (finding that cell-free fetal DNA methods are four times more sensitive than fetal cells for non-invasive prenatal screening for fetal chromosomal aneuploidy reveals that the latter is at least four times more sensitive). *See* Root Declaration, Exs. B, C, D, and E.

In *Ultramercial*, Chief Judge Rader summarized decades of Supreme Court Section 101 law and explained the bright line between patent-eligible subject matter and patent-ineligible matters, in that case an abstract idea:

> A claim can embrace [a patent ineligible matter] and be patentable. Instead, a claim is not patent eligible only if, instead of claiming an *application* of [a patent ineligible matter], the claim is instead *to* the [patent ineligible matter] itself. The inquiry here is to determine on which side of the line the claim falls: does the claim cover only [a patent ineligible matter], or instead does the claim cover an application of [a patent ineligible matter]?

Ultramercial, 2013 WL 3111303 at *7 (emphasis in original). *See also Bilski*, 130 S. Ct. at 3230 ("[W]hile an abstract idea, law of nature, or mathematical formula could not be patented, an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection."); *Diehr*, 450 U.S. at 187 ("It is now commonplace that an application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.").

The '540 patent is precisely this kind of patent-eligible exploitation of a natural phenomenon. It applies the natural phenomenon of cffDNA by combining previously known techniques in an innovative way to maternal plasma or serum in order to detect paternally inherited cffDNA for useful diagnostic purposes.

Ariosa's summary judgment motion also slides over the inventive importance of limiting detection to "paternally inherited" fetal DNA. While the use of cffDNA had overcome the technical problem of finding enough fetal cells to make reliable diagnoses, the cell-free DNA from the mother's plasma or serum was no longer just that of the fetus. Instead, the cell-free DNA was mostly that of the mother and much of the fetus's cell-free DNA was not readily distinguished from the mother's DNA. Drs. Lo and Wainscoat cleverly focused on the fetal DNA that would differ from the mother's DNA: first the Y chromosome, then the RhD gene in Rh-negative mothers, and detection of "*any* paternally-inherited sequences which are not possessed by the mother." '540 patent at 2:57-60 (emphasis added.)

Combining the inventive steps of starting with the mother's plasma or serum with the focus on paternally inherited DNA, the methods of the '540 patent are significantly more than the natural phenomenon that Drs. Lo and Wainscoat had discovered. Consistent with Supreme Court and Federal Circuit Section 101 law, this "application of a law of nature" is "deserving of patent protection."

2. In Light Of *Myriad*, The '540 Patent Does Not Fall Into The Natural Phenomenon Exception To Section 101.

The Federal Circuit vacated and reversed this Court's preliminary injunction ruling that had held there was "a substantial question" whether the '540 patent satisfied Section 101. *See Aria* at *6, reversing this Court's July 2, 2012 Order at 19. In arguing for affirmance, Ariosa extensively briefed *Prometheus*. Yet, the Federal Circuit did not find a "substantial question" on the Section 101 issue. Instead, the Federal Circuit vacated, reversed, and directed this Court on remand to re-consider its preliminary Section 101 ruling "in light of Myriad." *Aria* at *6. *Myriad* is the Supreme Court's latest word on Section 101.

In *Myriad*, the Supreme Court expressly carved out from Section 101 invalidity all claims to "new applications of knowledge" based on a natural phenomenon. 133 S. Ct. at 2119-20. The '540 patent involves only "applications of knowledge" claims, and accordingly satisfies Section 101.

In *Myriad*, the Supreme Court drew the line of patent ineligibility tightly around the BRCA genes' DNA sequences themselves, because they are naturally occurring phenomena. *Id.* at 2119. In contrast, the Supreme Court found that Myriad's claim to a method to isolate complementary DNA ("cDNA") "does not present the same obstacles to patentability as naturally occurring, isolated DNA segments." *Id.* "cDNA is not a 'product of nature,'" *id.*, and that distinction alone is sufficient to satisfy Section 101, without further analysis.

Thus, the Supreme Court invalidated claim 1 of Myriad's '282 patent which claimed "[a]n isolated DNA coding for a BRCA1 polypeptide . . . [with] the amino acid sequence set forth in SEQ ID No.2." *Id.* at 2113. This and similar claims describe the discovery of the natural

phenomenon and no more. The claims, "if valid, would give [Myriad] the exclusive right to isolate an individual's BRCA1 and BRCA2 genes." *Id*. According to the Supreme Court, "separating that gene from its surrounding genetic material is not an act of invention." *Id*. at 2117. But creating cDNA was "an act of invention." The Supreme Court held that "the lab technician unquestionably creates something new when cDNA is made." *Id*. at 2119. The area the Supreme Court carved out as patent-ineligible was very narrow, not extending to cDNA which Myriad had created from natural occurring sequences by entirely conventional methods. *Id.*

The methods of the '540 patent easily overcome the low bar for patent eligibility set by *Myriad.* The cffDNA itself is a natural phenomenon while in the mother's blood and, under *Myriad*, is therefore not patent-eligible. However, a method that instructs a technician to take a pregnant mother's plasma or serum, and amplify and then detect the paternally inherited DNA in that plasma or serum is "something new." By showing how to use this specific method for non-invasive sex determination and genetic diagnosis, including aneuploidy detection, the '540 claims meet the patent eligibility test of Section 101. The '540 patent therefore complies with Section 101 "in light of *Myriad.*"

Further, while there were no method claims before the Supreme Court in *Myriad*, the Court recognized that the natural phenomenon exception to patent eligibility does not invalidate methods based upon innovative uses of newly-discovered natural phenomenon. *See* 133 S. Ct. at 2119-20. The Court endorsed the notion that discoverers will often become inventors: "[A]s the first party with knowledge of the [genes'] sequences, Myriad was in an excellent position to claim applications of that knowledge. Many of its unchallenged claims are limited to such applications." 133 S. Ct. at 2120 (quoting *Ass'n for Molecular Pathology v. United States Patent and Trademark Office*, 689 F.3d 1303, 1349 (Fed. Cir. 2012) (Bryson, J., concurring in part and dissenting in part)).

Just as Myriad was free to patent applications of its discovery, the '540 patent's inventors, as "the first part[ies] with knowledge" that cell-free fetal DNA is present in maternal plasma and serum, were "free to patent applications of [their] discovery." 689 F.3d at 1349. In the '540

patent claims, Drs. Lo and Wainscoat made use of their discovery. Because the '540 patent does not claim the natural phenomenon of cffDNA, but instead claims specific uses of that discovery, those claims cross the Section 101 "threshold" for patent eligibility. *See Bilski*, 130 S. Ct. at 3225 (Section 101 is "a threshold test"); *Ultramercial*, 2013 WL 3111303 at *5 (Section 101 is "merely a threshold check").

This legal conclusion is still further reinforced by closer analysis of *Myriad*. The especially "apt" portion of Judge Bryson's opinion approvingly cited by the Supreme Court referenced several "unchallenged" method claims that Myriad had asserted in the litigation, including claim 21 of Myriad's U.S. Patent 5,753,441 ("'441 patent"). *See* 689 F.3d at 1349 ("As the first party with knowledge of the sequences, Myriad was in an excellent position to claim applications of that knowledge. Many of its unchallenged claims are limited to such applications. See, e.g., '441 patent, claim 21."). Directly analogous to the '540 patent's claims for a method to detect paternally inherited cffDNA from the mother's plasma, Myriad's claim 21 in its '441 patent recites a method for detecting a BRCA1 gene mutation:

> The method of claim 20 wherein a germline alteration is detected by hybridizing a BRCA1 gene probe which specifically hybridizes to an allele of one of said alterations to RNA isolated from said human sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said allele in the sample.

'441 patent (available at www.uspto.gov).

Myriad's claim 21 was patent-eligible even though it applied the conventional steps of hybridizing and detecting with probes on the naturally occurring BRCA1 gene that the inventors had discovered. This patentable subject matter in *Myriad* is conceptually indistinguishable from Sequenom's claims under the '540 patent, which, just like Myriad's claim 21, apply conventional techniques to detect and use a natural phenomenon for diagnostic purposes. "In light of *Myriad*," the '540 patent's claims pass Section 101 muster because they use the then-newly discovered natural phenomenon of cell-free fetal DNA to amplify and detect paternally inherited DNA sequences.

Ariosa ignores the Federal Circuit's direction that the '540 patent be re-considered in light of *Myriad.* Indeed, Ariosa's summary judgment brief gives little more than a passing reference to the Supreme Court's guidance in *Myriad*. *See, e.g.*, Ariosa Brief at 2. Ariosa notes the Supreme Court's holding that Myriad could not patent the specific DNA sequence of naturally occurring genes, but ignores entirely those aspects of *Myriad* that are pertinent here. Ariosa has nothing to say about *Myriad*'s validation that even conventional laboratory-manipulation of a newly discovered natural phenomenon is enough to make it patent eligible. Nor does it acknowledge that the Supreme Court endorsed the notion that the discoverers of a natural phenomenon are in the best position to invent patent-eligible methods to exploit that phenomenon. Nor does Ariosa discuss Myriad's Claim 21 of the '441 patent, which the Federal Circuit (and the Supreme Court) endorsed even though the method described in the claim applied well-known and widely-used techniques on the newly discovered natural phenomenon. Nor does it address the Supreme Court's appreciation that an innovative method that leads to discovery of a natural phenomenon may itself be patentable.

Reviewing the facts around the '540 patent in light of *Myriad* as the Federal Circuit directed, this Court should conclude that the invention is patent-eligible. It should therefore deny Ariosa's summary judgment motion and grant Sequenom's cross-motion.

3. In Light Of The Federal Circuit's Construction Of The '540 Patent's Claims, The Patent Describes An Inventive Method.

In *Prometheus*, the Supreme Court explained that the patent eligibility analysis "rests upon an examination of the particular claims . . . in the light of the Court's precedents." 132 S. Ct. at 1294. Consistent with that guidance, the Federal Circuit's opinion directed this Court to re-consider the Section 101 issue "in light of this court's disagreement with the district court's claim construction." *Aria* at *6. The panel made clear that the '540 patent claims a method to fractionate, to amplify paternally inherited fetal DNA (whether or not other nucleic acid is amplified), *see id.* at *5-6, and to detect paternally inherited cffDNA ("nucleic acid that originates from the fetus," "however or whenever it may be identified" to be "inherited from the father").

See id. at *3-5. While the Federal Circuit's constructions expressly rejected the limitations that Ariosa had encouraged this Court to include in the preliminary claim construction, these constructions do not claim cffDNA itself. These steps describe a specific method that requires use of maternal plasma or serum, mandates amplification of paternally inherited fetal DNA, and is limited to detection of paternally inherited cffDNA.

These constructions still leave the '540 patent readily distinguishable from the method that was found patent ineligible in *Prometheus*. The patent at issue in *Prometheus*, although purporting to be an innovative method, in fact did not change the method that had existed prior to the alleged "invention." The steps of the patent were administering a drug (thiopurine), determining the level of specific metabolites of that drug, and increasing or decreasing the dose of the drug based upon the levels of those metabolites. *See* 132 S. Ct. at 1297-98. Before the "invention," doctors routinely administered the drug, determined the levels of the metabolite, and adjusted the dose based upon the level of the metabolites. *Id*. What the inventors claimed was new was no more than a mental process – determining whether the patient's metabolite levels were above or below the precise cutoffs specified in the patent for increasing or decreasing the dose of drug. *Id.* at 1295-96. But the cutoffs were based upon a law of nature – how the body metabolizes the drugs – "an entirely natural process." *Id.* at 1297. Accordingly, the Supreme Court held that Prometheus' patent claimed nothing more than an unpatentable law of nature.

In contrast to *Prometheus*, the '540 patent revolutionized non-invasive prenatal diagnosis. Where previously researchers had tossed out the pregnant mothers' plasma and serum, Drs. Lo and Wainscoat seized upon it as a new source for detectable quantities of fetal DNA. The '540 patent claimed methods of using maternal plasma or serum by amplifying and detecting paternally inherited fetal DNA. The inventors of the '540 patent used these methods to detect portions of the Y chromosome in pregnant women, DNA that the fetus had inherited from his father. *See Aria* at *3. Similarly, they detected portions of the RhD gene in plasma of pregnant women who ostensibly did not have the RhD gene. *See id.* at *4. RhD gene sequences should have been present in the mother's plasma or serum only if the fetus had inherited that gene from

his or her father. *Id.* These experiments allowed the inventors to confirm their hypothesis that there was cffDNA in pregnant mothers' plasma and serum.

Then, having established that cffDNA existed in the plasma of pregnant mothers in detectable quantities, the inventors' method could be used to detect paternally inherited fetal DNA in the pregnant mother's plasma or serum. *Id*. The Federal Circuit emphasized, there was "no limitation whatsoever" on the term "paternally inherited" suggested by "the single sentence in the specification on this topic . . . the 'method according to the invention can be applied to the detection of *any* paternally-inherited sequences which are not possessed by the mother.'" *Id.* at *3 (quoting '540 patent at 2:57-60 (emphasis added)).

This opened up a new frontier of non-invasive prenatal diagnosis. This specific inventive method involving a particular combination of elements "in practice amounts to significantly more than a patent upon the natural law itself." *Prometheus*, 132 S. Ct. at 1294. Because the '540 patent claims a use of a natural phenomenon rather than merely the natural phenomenon itself, its methods are patent eligible.

Ariosa misreads *Prometheus* when it argues that the '540 patent merely added to the natural phenomenon of cffDNA, "well-understood, routine, conventional activity previously engaged in by researchers in the field." Ariosa Brief at 3 (quoting *Prometheus*, 132 S. Ct. at 1294). What was "well-understood, routine, conventional activity previously engaged in by researchers in the field" in *Prometheus* was the very method that Prometheus was trying to claim – administering the drug, measuring metabolite levels and adjusting dosing based upon the metabolite levels.

The '540 patent contrasts starkly with the patent in *Prometheus.* Before the *Prometheus* patent, doctors were already administering the drug, measuring metabolite levels, and adjusting dosage based upon metabolite levels. *See* 132 S. Ct. at 1297-98. Before the '540 patent, *no one* was using the plasma or serum of pregnant mothers to amplify and detect paternally inherited fetal DNA.

The *Prometheus* Court "reinforce[d]" its conclusion that Prometheus was claiming an unpatentable subject matter with a "detailed consideration of the controlling precedents" "most

directly on point." 132 S. Ct. at 1298 (citing *Diamond v. Diehr*, 450 U.S. 175 (1981), and *Parker v. Flook*, 437 U.S. 584 (1978)). In *Flook*, on the one hand, the Court held that an invention that introduced a new algorithm to the pre-existing process of a catalytic converter was unpatentable because "[t]he only difference between the conventional methods . . . and that described in [the inventor's] application rests in . . . the mathematical algorithm." *Flook*, 437 U.S. at 585-86. The claim in *Diehr*, on the other hand, was patentable because it provided a new method for curing rubber using a particular equation that uses temperature to set cure time. *See* 450 U.S. at 184. In the prior art, the equation was calculated at the outset of the process, while the inventors in *Diehr* claimed a process "of constantly measuring the actual temperature." 450 U.S. at 178.

Considering these precedents, the claims of the '540 patent are patent eligible because they constituted a substantial change from the then conventional method of non-invasive prenatal genetic diagnosis. The '540 patent is more like the *Diehr* patent than the *Flook* patent. No previous researchers had used maternal plasma or serum to detect paternally inherited fetal DNA. Indeed, previous research in the field of non-invasive prenatal genetic diagnosis had used rare fetal cells found in the mother's blood stream. *See Aria* at *1. Because those efforts discarded the maternal plasma and serum, *id*., the earlier work *taught away* from the detection method claimed in the '540 patent. Simply put, at the time the '540 patent's claimed method was invented, its steps for detection of paternally inherited cffDNA in maternal serum or plasma were, contrary to Ariosa's argument, neither "well-understood" nor "routine" nor "conventional activity" to "researchers in the field."

Just as widespread praise, unexpected results, unsolved needs, and prior art that teaches away may show a claimed invention to be non-obvious under Section 103, *see United States v. Adams*, 383 U.S. 39, 51-52 (1966); *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 18 (1966), so too should these factors weigh in favor of finding that the application of known steps in a new way constitutes an "inventive concept," rendering a patent valid under Section 101.

Ariosa tries to rely on two snatched-from-context snippets of the prosecution history to argue that the '540 inventors understood their discovery of cffDNA to be the only thing novel about their invention. *See, e.g.*, Ariosa Brief at 2, 9. The snippets say nothing of the sort.

The first snippet says that starting with the mother's plasma or serum is a "particular[ly]" "key feature" of the invention. That is an accurate statement – the prior method threw away that plasma or serum. The '540 patent patent taught how to use the plasma or serum. Ariosa also ignores the inventive aspect of limiting the claim to "paternally inherited" fetal DNA. The prior art had relied upon finding rare fetal cells where the DNA was just that of the fetus. In using the cell-free DNA in the maternal plasma or serum, Drs. Lo and Wainscoat recognized that they needed a means of distinguishing cffDNA from the background of the mother's own cell-free DNA. Focusing on paternally inherited DNA provided a way to do that.

The second snippet is similarly unenlightening. The inventors describe the fact that the plasma or serum contains "large amounts of fetal nucleic acid" as "in itself, the solution to a significant technical problem." The specification, in fact, goes to great lengths to explain that starting with maternal plasma or serum rather than the tradition hunt for fetal cells means that there is nearly a 1,000-fold increase in the relative frequency of fetal to maternal material. *See* '540 patent at 16:28-30. None of that changes the simple fact that before the invention, no one was doing what '540 patent is claiming: using the maternal plasma or serum to detect fetal DNA.

In any event, whether a patent satisfies Section 101 is not based on how the inventor describes the invention, but what the patent actually claims. *See Prometheus*, 132 S. Ct. at 1294. The '540 patent, as construed by the Federal Circuit, does not claim a natural phenomenon, but claims only a novel and inventive method to apply and use it. In *DDR Holdings, LLC. v. Hotels.com, L.P.*, __ F. Supp. 2d __, 2013 WL 3187161 (E.D. Tex. June 20, 2013), the court also confronted supposed "inventor admissions" that the patent was limited to patent ineligible subject matter. In *DDR*, the infringer argued that the patent was an abstract idea and thus not patent eligible under Section 101, relying on the inventor's testimony in which he had referred "25 times" to his invention as an "idea." 2013 WL 3187161 at *16. The district court found that this testimony "is not instructive . . . for purposes of § 101 patentability" because "it is not unusual to explain a patent claim as a 'gist' or 'core idea'" and "'all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas.'" *Id*. at *16 (quoting *Prometheus*, 132 S. Ct. at 1293).

Thus, when this Court reconsiders the Section 101 question in light of the Federal Circuit's disagreements with this Court's preliminary claim construction, this Court should conclude that the '540 patent satisfies Section 101.

C. THE '540 PATENT DOES NOT PREEMPT THE PRACTICAL USE OF CFFDNA.

The Supreme Court and the Federal Circuit have emphasized that the aim of the exceptions to Section 101 is to prevent the monopolization of unpatentable laws of nature, natural phenomena, and abstract ideas. Ariosa buries at the end of its brief the issue of whether the '540 patent monopolizes the use of cffDNA. Ariosa argues that it makes no difference whether the patent preempts other uses of the natural phenomenon. That is a misstatement of the law. Preemption analysis is fundamental to deciding whether Section 101 is met. As explained below, the '540 patent has important limitations that prevent its claims from preempting all use of cffDNA. For this reason too, the Court should deny Ariosa's motion and grant Sequenom's cross-motion.

As the Supreme Court explained in *Prometheus*: "If a law of nature is not patentable, then neither is a process reciting a law of nature, unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." 132 S. Ct. at 1297. In *Prometheus*, the Supreme Court emphasized that Section 101 could not be satisfied if the patent's claims "disproportionately t[ie] up the use of the underlying natural laws, inhibiting their use in the making of further discoveries." *Id.* at 1294.

The Supreme Court in *Prometheus* held that its method monopolized the use of metabolites to determine the proper dose of thiopurine because the physical steps in the patent added no meaningful limitation. The only place where Prometheus' new cutoffs would be useful was when the doctor had administered the drug and measured the metabolite levels. *Id*. at 1297-98. At the same time, the new element – the cutoffs for increasing and decreasing the dose – was purely a mental step. *Id*. at 1297. Under Prometheus' own construction, "a doctor using Mayo's test could violate the patent even if he did not actually alter his treatment decision in light of the

test." *Id.* at 1296. That meant that Prometheus was claiming a monopoly over all uses of the law of nature that connected the dose of the drug to the metabolite levels. Accordingly, the Supreme Court found that the patent in *Prometheus* was not patent eligible.

As with other aspects of its holding in *Prometheus,* the Supreme Court "reinforce[d its] conclusion" on preemption by a "detailed consideration of the controlling precedents," notably *Diehr* and *Flook.* 132 S. Ct. at 1298. The patents in both decisions involved the application of mathematical equations to industrial processes, with the claims in *Diehr* held patent eligible and the *Flook* claims held patent ineligible. *Prometheus* found the pre-emptive effect of the claims to be a critical distinction between the cases. *Id*. at 1298-99. In *Diehr,* "the patentees did not 'seek to pre-empt the use of [the] equation' but sought 'only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.'" *Prometheus,* 132 S. Ct. at 1299 (quoting *Diehr,* 450 U.S. at 187.) In contrast, in *Flook*, beyond the equation, "the other steps in the process did not limit the claim to a particular application." *Prometheus,* 132 S. Ct. at 1299 (citing *Flook,* 437 U.S. at 586).

Since *Prometheus*, the Federal Circuit has reiterated that preemption is the critical issue in determining patent eligibility. Nine of the ten judges in the Federal Circuit's en banc *CLS Bank* decision endorsed the use of preemption analysis to determine Section 101 patent eligibility.[3] As Judge Lourie's plurality opinion in *CLS Bank* states, "the Supreme Court's foundational §101 jurisprudence . . . turns primarily on the practical likelihood of a claim preempting a fundamental concept." 717 F.3d at 1277. "First and foremost is an abiding concern that patents should not be allowed to preempt the fundamental tools of discovery. . . . Guarding against the wholesale preemption of fundamental principles should be our primary aim in applying the common law exceptions to § 101. . . . What matters is whether a claim threatens to subsume the full scope of a fundamental concept. . . ." *Id.* at 1280-81. Chief Judge Rader's concurring opinion also reaffirms

[3] In the appeal of this Court's July 2, 2012 order before the Federal Circuit, Ariosa relied on the three-judge panel's opinion in *CLS Bank,* which denied that preemption was an "essential concern" in §101 analysis. *See* Ariosa Responding Brief to Federal Circuit (Nov. 9, 2012) at 23. The Federal Circuit's *en banc* opinion in *CLS Bank* has since held otherwise.

that a Section 101 eligibility problem arises only "when a claim preempts all practical uses of an abstract idea." *Id*. at 1300.

Preemption analysis is dispositive of the Section 101 issue here. The '540 patent claims do not preempt all other uses of cell-free fetal DNA in maternal blood. For example, the '540 patent does not preclude methods that make use of cffDNA without separating out the maternal plasma or serum**.** Researchers, including Ariosa's own expert Dr. Bischoff, have developed systems to detect cell-free fetal DNA from whole maternal blood without removing the cellular component. A2011-2012 at 107:3-108:12; A2036-2037 at 178:2-179:21; A2102-2105; A1875-1876, ¶ 27. In her paper, Dr. Bischoff argued that, compared to a method (like the '540 patent) involving fractionation, her method may be "better due to absence of anticoagulant" and could allow "a simple method for transport and collection, enabling cell-free fetal DNA to be incorporated into non-invasive screening regimes." A2104.[4] The availability of such non-fractionation methods allows use of the underlying natural phenomenon by others, without infringement of the '540 patent. *Compare Prometheus*, 132 S. Ct. at 1301.

Similarly, as construed by the Federal Circuit, the '540 patent requires the amplification of paternally inherited fetal DNA. *See Aria* at *5-6. This does not preempt methods that involve no amplification, such as that described in a recent peer-reviewed journal. *See* A1875 ¶ 26; Jessica M.E. van den Oever et al., *Single Molecule Sequencing of Free DNA from Maternal Plasma for Noninvasive Trisomy 21 Detection*, 58 Clinical Chemistry 657, 699-706 (2012) (at A2273-2280). According to the article, a single-molecule genetic sequencing technology involving no amplification has been used for the non-invasive detection of trisomy from cffDNA, reflecting an alternative application of the natural phenomenon from that used in the Sequenom and Ariosa tests. *Id.*

[4] Ariosa is wrong when it argues that "any method that makes use of whole blood would not be using the natural phenomenon at issue in this case." Ariosa Br. at 23 n.5. Dr. Bischoff used cffDNA in her experiment even though she started with whole blood without isolating a cell-free fetal fraction. *See* A2102-2105; A1875-1876, ¶ 27.

Additionally, as construed by the Federal Circuit, the '540 patent is limited to the detection of paternally inherited DNA. *See Aria* at *3-5. The peer-reviewed literature has reported experiments using methods that look for fetal markers to identify cffDNA without distinguishing between paternally inherited and maternally inherited DNA.[5] The '540 patent does not preempt methods that never distinguish whether specific fetal DNA was inherited from the mother or the father.

The undisputed evidence is that the '540 patent does *not* preempt nor monopolize *all* uses of cffDNA. Each of the limitations of claim 1 of the '540 patent confines the claim to a combination of specific steps for using cell-free fetal DNA, leaving open other approaches to use that natural phenomenon. Because those limitations are meaningful, they are not an "artifice." *See* Ariosa Brief at 2. Those limitations are incorporated into each of the other claims that Sequenom is asserting against Ariosa, either by being dependent on claim 1 or, as in claims 24 and 25, by restating those limitations.

Because it must defeat every dependent claim to win summary judgment, Ariosa spends a substantial portion of its brief analyzing each of the '540 patent's dependent claims asserted against Ariosa. However, Ariosa avoids any consideration of the additional *limitations* in those claims. For example, claim 2 requires that paternally inherited nucleic acid is amplified by the polymerase chain reaction ("PCR"). PCR requires the use of "primers" to hybridize with the nucleic acid to be amplified. The PCR process is not a natural phenomenon and was itself patented. *See* U.S. Patent No. 4,683,202 (available at www.uspto.gov). Yet, PCR is just one of several methods that can be used to amplify nucleic acids. While claim 1 of the '540 patent requires the amplification of paternally inherited nucleic acid from the plasma or serum sample, the additional limitation of the amplification step in claim 2 to only PCR takes the patent still further from monopolizing the field.

[5] *See, e.g.*, Leo L. Poon, *Differential DNA Methylation Between Fetus and Mother as a Strategy for Detecting Fetal DNA in Maternal Plasma*, 48 Clinical Chemistry 9, 35-40 (2002). *See* Root Declaration, Ex. F.

Similarly, dependent claim 4 requires that the paternally inherited foetal nucleic acid is detected by means of a sequence-specific probe. Claim 4 alone would not reach other methods of detecting paternally inherited nucleic acid that do not use a sequence-specific probe. Likewise, claims 5 and 8 add further restrictions that the paternally inherited nucleic acid detected must be from the Y chromosome and non-Y chromosomes respectively, again further limiting the scope of those claims compared to claim 1. Claims 19 to 22 also add limitations to the scope of claim 1. Thus, contrary to Ariosa's arguments, all the asserted dependent claims pass muster under section 101 and none of them monopolizes all uses of cffDNA.

Ariosa has not produced evidence, let alone clear and convincing evidence, that the '540 patent claims "disproportionately t[ie] up the use of the underlying natural laws, inhibiting their use in the making of further discoveries." *Prometheus*, 132 S. Ct. at 1294. Because others have exploited cffDNA in ways not preempted by the '540 patent, and future inventors may be able to do so in other novel ways not yet devised, Ariosa has failed to present clear and convincing evidence that the'540 patent monopolizes the use of cffDNA. Consequently, the Court should hold that the '540 patent's method draws on patent-eligible subject matter under Section 101.

D. THE '540 PATENT'S METHOD IS AN INNOVATIVE USE OF A NOVEL COMBINATION OF VARIOUS CONVENTIONAL TECHNIQUES

Ariosa devotes nearly half of its brief to showing that each of the steps of the various claims in the '540 patent were well known in the art prior to the invention. Ariosa Brief at 10-22. However, this argument ignores the unprecedented use of these steps *in combination* to detect paternally inherited fetal DNA. In context, and as its claims have been construed by the Federal Circuit, the '540 patent's method is novel, unconventional, contrary to the scientific knowledge of the time, and a marked departure from the work of others in the field. A1118-1119, ¶¶ 69-71.

Ariosa's argument also ignores the law. The Supreme Court and the Federal Circuit have repeatedly held that Section 101 eligibility is not at risk just because each of the individual steps of a patented method may have been known in the art and been previously used in other contexts. In *Diehr*, the Supreme Court held that Section 101 permits a patent that uses the inventive

combination of known and conventional techniques in a method or process to unlock the commercial use of a natural phenomenon. According to the Supreme Court,

> This is particularly true in a process claim because a new combination of steps in a process may be patentable even though all the constituents of the combination are well known and in common use before the combination was made. The 'novelty' of any element or steps in a process, or even of the process itself, is of no relevance in determining whether the subject matter of a claim falls within the § 101 categories of possibly patentable subject matter.

450 U.S. at 188-89. In *Diehr*, the Supreme Court explicitly *disapproved* of the item-by-item dismantling of a method's elements that Ariosa follows in its brief:

> It is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis. . . . To accept the analysis proffered by the petitioner would, if carried to the extreme, make all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious.

Id. at 188-89 & n.12.

Ariosa would have this Court read *Prometheus* as overruling *Diehr* and other cases that disapproved of the step-by-step dismantling of a method. To the contrary, *Prometheus* reiterated that earlier law. For example, the Supreme Court explained that "a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made." 132 S. Ct. at 1298 (citing *Diehr*, 450 U.S. at 188).

It is not appropriate to strip away all of the "conventional" limitations of the patent, and then argue that at its core, the patent is claiming only a natural phenomenon or an abstract idea. As the Federal Circuit recently explained post-*Myriad*:

> [A]ny claim can be stripped down, simplified, generalized, or paraphrased to remove all of its concrete limitations, until at its core, something that could be characterized as an abstract idea is revealed. A court cannot go hunting for abstractions by ignoring the concrete, palpable, tangible limitations of the invention the patentee actually claims.
>
> Instead, the relevant inquiry is whether a claim, as a whole, includes *meaningful* limitations restricting it to an application, rather than merely an abstract idea.

Ultramercial, 2013 WL 3111303 at *8.

Yet, Ariosa makes precisely this improper argument by asserting that the '540 uses "the artifice of grafting non-inventive activities onto [a natural] phenomenon." Ariosa Brief at 2. Ariosa ignores the appropriate inquiry – whether it was standard or conventional to *apply this combination of fractionation/amplification/detection techniques to cell-free fetal DNA*. Here, by innovatively combining techniques that may have been "standard" in other contexts, and applying that novel combination in an unexpected and new manner specifically to paternally inherited cffDNA, Drs. Lo and Wainscoat invented a patentable method that satisfies Section 101.

IV. CONCLUSION.

For the reasons stated above, this Court should deny Ariosa's motion for summary judgment and hold that the '540 patent is patent eligible under 35 U.S.C. § 101.

For these reasons too, the Court should grant Sequenom's cross-motion for partial summary judgment and strike Ariosa's affirmative defense of invalidity under Section 101.

Dated: September 4, 2013

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